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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,578	07/22/2003	Lars Blank	030307-0217	6542

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EXAMINER	
ARIANI, KADE	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/623,578	BLANK ET AL.	
	Examiner	Art Unit	
	Kade Ariani	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 31-47 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 31-47 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendments filed on February 05, 2007, has been received and entered.

Claims 1-30 have been canceled.

Claims 31-47 are pending in this application and were examined on their merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over de Vos (Antonie van Leeuwenhoek 1996, Vol.70, p.223-242) in view of Sijpesteijn (Antonie van Leeuwenhoek 1970, Vol.36, p.335-348) and further in view of Wessels et al. (US Patent No. 5,580,787).

Claims 31-47 are drawn to a culture of lactic acid bacterial cells that are characterized by a reduced glycolytic flux and, under aerobic conditions, a respiratory metabolism, whereby said culture displays a yield of biomass exceeding that obtainable from substrate-level phosphorylation, wherein (i) said reduced glycolytic flux is provided by introducing mutations in said cells to generate a lower rate of metabolism of the carbon source and (ii) said respiratory metabolism is provided by introducing

manipulations to said cells to produce an increased yield of ATP in said cells via oxidative phosphorylation when said cells are propagated in the presence of a terminal electron acceptor, starter culture comprising the lactic acid bacterial culture, the composition is frozen, a bacterial nutrient or cryoprotectant, 10^4 to 10^{12} CFU/g, cells contain at least 0.1 ppm on a dry matter basis of cytochrome, and two or more different lactic acid bacterial strains.

De Vos teaches metabolic engineering for rerouting sugar metabolism in lactic acid bacteria (see Abstract and the rest of the article), batch culture of lactic acid bacteria (p.232, Col.2 second paragraphLines15- 16), flux from pyruvate was rerouted from lactate in *Lactobacillus plantarum* mutants grown under aerobic conditions on glucose (p.234, Col.1, lines 17-21), studies shown that lactic acid bacteria show a greater metabolic potential when the reduced cofactors from which NADH is the most important are regenerated by exogenous electron acceptors (cytochrome) (p.236, Col.1, second paragraph, lines), mutations in *lac* operon and its repressor (p.227, Col.1 Lines 4-11 and Table 2.), de Vos further teaches sugar transport systems exert significant control of the flux in a catabolic pathway, and genes involved in sugar transport are located in clusters or operons that also code for sugar-specific catabolic reactions (p.226, Col.1, lines 9-3, and p.228, Figure 2). Thus, one would have been motivated to increase the yield of biomass in a culture of lactic acid bacterial cells by increasing the activity of the enzymes involved in the uptake or degradation of a carbon source.

De Vos does not teach a starter culture comprising the lactic acid bacterial culture, the composition is frozen, a bacterial nutrient or cryoprotectant, 10^4 to 10^{12}

CFU/g, cells contain at least 0.1 ppm on a dry matter basis of cytochrome, and a composition of two or more different lactic acid bacterial strains. However, Sijpesteijn teaches induction of cytochrome formation by adding hemin to an overnight grown lactic acid bacterial cell culture (see abstract and Material & Methods), the formation of cytochrome a_2 and a cytochrome b (p.344, lines13-15 and Table 5).

Moreover, Wessels et al. teaches preparing starter cultures comprising lactic acid bacteria into which desired genes have been introduced (see abstract), use of starter cultures comprising a multiplicity of selected lactic acid bacterial strains each having one or several of the characteristics desirable for a particular food product (Col.1 Lines 55-61). Also at the time the invention was made adding glycerol (cryoprotectant) prior to freeze-drying the cells to enhance the viability of bacterial cells during storage was very well known in the art.

Therefore, in view of the above teachings, it would have been obvious to one the ordinary skill in the art to introduce mutations to a lactic acid bacterial species in order to obtain a culture that displays a yield of biomass exceeding that obtainable from substrate level phosphorylation under aerobic conditions and to produce an increased yield of ATP via oxidative phosphorylation by propagating cells in the presence of a terminal electron acceptor. One would have been motivated to do so, because enabling respiration in a lactic acid bacterial strain would provide a more efficient conversion of the available carbon source to biomass resulting to higher yields and increased survival following growth and both these properties are of industrial significance. There would have been a reasonable expectation of success because at the time the invention was

made it was very well known that adding a terminal electron acceptor to a culture of lactic acid bacterial cells induce cytochrome formation and respiration.

Accordingly, the invention taken as whole is *prima facie* obvious.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on 9:00 am to 5:30 pm EST Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kade Ariani
Examiner
Art Unit 1651

Leon B. Lankford Jr.
Primary Examiner
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